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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/747,715	12/26/2003	Michael Christopher Montalto	133658-2	5857

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GENERAL ELECTRIC COMPANY
GLOBAL RESEARCH
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EXAMINER	
JONES, DAMERON LEVEST	
ART UNIT	**PAPER NUMBER**
1618	

DATE MAILED: 08/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/747,715	MONTALTO ET AL.	
	Examiner	Art Unit	
	D. L. Jones	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/5/06 1/10/05 3/9/06 2/14/06 &7/19/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-81* is/are pending in the application.

4a) Of the above claim(s) *65,66,73,75 and 81* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-64,67-72,74 and 76-80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/10/05; 3/9/06; &.* 7/19/06
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

ACKNOWLEDGMENTS

1. The Examiner acknowledges receipt of the amendment filed 2/14/06 wherein claims 1-57 were canceled and claims 58-81 were added.

Note: Claims 58-81 are pending.

APPLICANT'S INVENTION

2. Applicant's invention is directed to methods of assessing an amyloid related disease as set forth in independent claims 58 and 69.

RESPONSE TO APPLICANT'S ELECTION

3. The Examiner acknowledges Applicant's election of the species wherein the disease is Alzheimer's; the imaging agent comprises an antibody; the label and detection method is by positron emission tomography using a compatible isotope; and the A beta peptide comprises oligomers of up to 24 A beta peptides.

Note: The search was not expanded beyond Applicant's elected species because prior art was found which could be used to reject the instant invention. In addition, it should be noted that Applicant's election was made without traversal. Thus, the election of species requirement is deemed as proper and is made FINAL.

WITHDRAWN CLAIMS

4. Claims 65, 66, 73, 75, and 81 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected species.

112 FIRST PARAGRAPH REJECTION (New Matter/Written Description)

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 58-64, 67-72, 74, and 76-80 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims contain new matter and the disclosure lack written description because the originally filed claims and disclosure were directed to compounds of Formula I (see pages 2-3) and imaging agents where were comprised of the compounds of Formula I and a label. Hence, the claims as now presented read on species which were not envisioned by the disclosure as originally filed.

Furthermore, Applicant only discloses Alzheimer's disease in the instant invention (see specification, page 3, paragraph [0012], and originally filed claim 46) as disease for which the instant invention is applicable. Hence, the claims lack written description and contain new matter because the pending claims encompass subject matter that was not envisioned by the disclosure as originally filed.

112 FIRST PARGRAPH REJECTION (Scope of Enablement)

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 58-64, 67-72, 74, and 76-80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Alzheimer's disease, does not reasonably provide enablement for all amyloid related diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are several guidelines when determining if the specification of an application allows the skilled artisan to practice the invention without undue experimentation. The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are (1) nature of the invention; (2) state of the prior art; (3) level of one of ordinary skill in the art; (4) level of predictability in the art; (5) amount of direction and guidance provided by the inventor; (6) existence of working examples; (7) breadth of claims; and (8) quantity of experimentation needed to make or use the invention based on the content of the disclosure.

(1) Nature of the invention

The claims are directed to methods of assessing an amyloid related disease as set forth in independent claims 58 and 69.

(2) State of the prior art

The references of record do not indicate all possible amyloid related diseases for which the instant invention is compatible. However, the references disclose that

imaging agents may be utilized in the detection of amyloid plaques in subjects with Alzheimer's disease.

(3) Level of one of ordinary skill in the art

The level of one of ordinary skill in the art is high. Independent claims 58 and 69 encompass a vast number of possible amyloid related diseases and imaging agents. Applicant's specification does not enable the public to make or use such a vast number of possible imaging agents or identify the amyloid related disease/diseases because the disclosure is directed to compounds of Formula I, not an unlimited number of compounds (imaging agents) as set forth in the pending claims.

(4) Level of predictability in the art

The art pertaining to assessing amyloid related diseases and imaging agents associated therewith is highly unpredictable. Determining the various types of diseases and imaging agents or class of diseases and imaging agents that are compatible with all amyloid related conditions requires various experimental procedures and without guidance that is applicable to all amyloid plaques, there would be little predictability in performing the claimed invention. For example, see Wu et al (J. Clin. Invest., 1997, Vol. 100, pages 1804-1812) which disclose that whiled one may have radiolabeled A-beta 1-40, the absence of a component that crosses the blood brain barrier results in a radiopharmaceutical useful for in vitro, not in vivo purposes, . Hence, there is little predictability in performing the claimed invention, absent some guidance, since some while an imaging agent may be used for in vitro purposes, obstacles may prevent it from

being used in vivo. Thus, one needs to clearly set forth the imaging agents and diseases for which the instant invention is being used.

(5) Amount of direction and guidance provided by the inventor

Independent claims 58 and 69 encompass a vast number of diseases and imaging agents. Applicant's limited guidance does not enable the public to prepare such a numerous amount of imaging agents for used with various amyloid related diseases. There is no directional guidance for the diseases or imaging agents compatible with the instant invention other than compounds of Formula I as set forth in the specification. Hence, there is no enablement for all possible permutations and combinations of imaging agents and amyloid related diseases.

(6) Existence of working examples

Independent claims 58 and 69 encompass a vast number of disease and imaging agents. Applicant's limited working examples do not enable the public to prepare such a numerous amount of diseases and imaging agent combinations. While Applicant's claims encompass a plethora of possible diseases and imaging agent combinations, the specification provides for only Alzheimer's disease and imaging agents of Formula I which contains a label.

(7) Breadth of claims

The claims are extremely broad due to the vast number of possible diseases and imaging agents known to exist.

(8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure

The specification does not enable any person skilled in the art to which it pertains to make or use the invention commensurate in scope with the claims. In particular, the specification fails to enable the skilled artisan to practice the invention without undue experimentation. Furthermore, based on the unpredictable nature of the invention, the state of the prior art, and the extreme breadth of the claims, one skilled in the art could not perform the claimed invention without undue experimentation.

112 SECOND PARAGRAPH REJECTION

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 58-64, 67-72, 74, and 76-80 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims as written are ambiguous because one cannot readily ascertain what is being claimed. Specifically, the claims as written read on various imaging agents and amyloid related diseases. However, one of ordinary skill in the art would not be able to ascertain what is encompassed in the claim as written. In particular, the claims as written are ambiguous because it is unclear what specific imaging agents or groups of imaging agents are compatible with the instant invention. Likewise, it is unclear what amyloid related disease/diseases Applicant is claiming which are compatible with the instant invention. Applicant is respectfully requested to clarify the claim in order that one may determine what is being claimed.

103 REJECTIONS

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 58-64, 67-72, 74, and 76-80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al (J. Clin. Invest., 1997, Vol. 100, pages 1804-1812).

Wu et al disclose drug targeting of a peptide radiopharmaceutical through the primate blood brain barrier in vivo with a monoclonal antibody to the human insulin receptor. Radiolabeled (125I) A-beta1-40 was monobiotinylated and conjugated to a blood brain barrier drug delivery and brain targeting system comprised of a complex of 83-14 monoclonal antibody which is tagged with streptavidin. After intravenous injection, there was a marked increased in rhesus monkey brain uptake of the radiolabeled pharmaceutical (see entire document, especially, abstract; pages 1805-1806, 'Methods'; page 1807, Figure 5; page Figure 6; page 1809, Figure 8; page 1809, Figure 9; and page 1810, Figure 11). The A-beta amyloid of tissue sections of Alzheimer's disease can be identified with dyes such as Congo Red or with antibodies directed against certain epitopes of A-beta 1-42/43 peptide. Thus, radiolabeled A-beta 1-40 is a peptide radiopharmaceutical useful for neurodiagnostic quantification of the A-beta amyloid burden in Alzheimer's disease brain of living subjects using standard external detection methodologies such as positron emission tomography (page 1804,

column 2, second complete paragraph; pages 1804-1805, bridging paragraph). Hence, both Applicant and Wu et al disclose methods of assessing an amyloid related disease, Alzheimer's disease, comprising administering a subject an imaging agent that binds to A-beta and detecting the imaging agent. However, while Wu et al does not specifically state that the A-beta being detected is soluble, the skilled practitioner in the art would recognize that plaques are composed of insoluble and soluble components. This position is supported by Applicant's disclosure (see Background of the Invention, page 1, paragraph [0003]) which discloses that it is known that plaques are composed mainly of deposited (or insoluble in an aqueous solution) fibrillar forms of beta amyloid (A-beta) peptide. However, recently it has been shown that soluble oligomers (soluble in aqueous buffer) of A-beta could contribute significantly to neuronal dysfunction (see Back of the Invention, page 1, paragraph [0003]). Furthermore, it is noted that Applicant has defined 'A-beta species' as used in the specification to refer to A-beta soluble monomers, soluble oligomer, and insoluble fibrils (see Detailed Description, page 4, paragraph [0013]). Hence, the phrase encompasses both insoluble and soluble A-beta components

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (571) 272-0617. The examiner can normally be reached on Mon.-Fri., 6:45 a.m. - 3:15 p.m.. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor,

Michael Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

D. L. Jones
Primary Examiner
Art Unit 1618

August 18, 2006